Trichloroethylene

CAS #79-01-6
F344 rats, at 0.0, 0.15, 0.30, and 0.60% in feed
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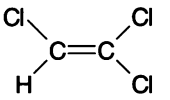

Trichloroethylene (TCE), a common industrial solvent and dry cleaning agent, was tested for its effects on reproduction and fertility in Fischer 344 rats using the RACB protocol (Morrissey et al., Fundam Appl Toxicol 13:747–777 [1989]). TCE was microencapsulated in a gelatin/sorbitol shell, and added to the diet. Data from a two week dose-range-finding study (Task 1) were used to set exposure concentrations for the Task 2 continuous cohabitation study at 0.15, 0.30, and 0.60% weight per weight. Based on the results of the analysis of feed formulations and measures of feed consumption, the daily TCE dosages were approximately 76, 156, and 289 mg/kg/day.

In the F_0 animals, there were no clinical signs of toxicity, and no animals died during the Task 2 phase. Dam postpartum body weights were reduced at all dose levels during Task 2: from 4 to 6% at the low dose to approximately 8% at the high dose. There was a monotonic trend to fewer litters per pair (from 3.5 in controls to 2.9 in the high dose group), although the pairwise comparison was not statistically significant. The middle and high dose groups had 9 and 16% fewer pups per litter than the controls. Pup weight and viability were unchanged at any dose level.

The last litter was reared by the dam. During this 21-day nursing period, viability was not affected by TCE exposure, but body weights were depressed for pups from all treated groups. The decrease was not dose-related, and ranged from 9 to 20% compared to controls. At 21 and 45 days postpartum, the F_1 rats from all groups were tested for behavioral alterations in an open-field test. At 21 days there were no differences across groups, while at 45 days, mice at the high dose crossed the field fewer times, each trip was quicker than controls, and there were fewer rearing episodes, and more time spent grooming.

The changes in fertility and pup number seen in Task 2 prompted the conduct of a Task 3 crossover to determine the affected sex using the control and top dose groups. While 100% of the control × control pairs mated, only 75% of the groups containing a treated animal did. There were no differences across groups in terms of the number of pups per litter, or the viability or weight of those pups. An affected sex could not be determined for this compound.

After the delivery and assessment of the Task 3 litters, the control and high dose F_0 adults were killed and necropsied. The body weight of high dose treated males was reduced by approximately 4%, while relative liver weight and kidney weight was increased by approximately 24 and 12%, respectively, compared to controls. There were no changes in sperm indices. For females, body weight was reduced by approximately 10%, while relative liver weight was increased by approximately 19% and kidney weight was increased by approximately 7%.

The fertility of the second generation was evaluated for all dose groups. There was no treatment-related effect on the proportion of pairs mating or delivering litters, nor were there any differences between the groups in terms of number of pups per litter, or pup viability or weight.

After delivery and evaluation of the F_2 pups, the F_1 adults were killed and necropsied. Male body weights were reduced by 5, 7, and 9% (low to high dose groups, respectively). Absolute testis weight was also reduced by 6 to 8% in all dosed groups. Adjusted liver weights were increased by 6, 9, and 16%, respectively. Seminal vesicle weight was increased by approximately 18% at the middle dose only. Treated female body weights were reduced by 4, 3, and 11%, respectively, from low to high dose groups, while adjusted liver weight was increased by 10% at both the middle and high dose levels. Abnormal sperm forms were more numerous at the low dose, approximately doubled from 0.54 to 1.13%. No other sperm changes were noted. No vaginal cyclicity data were collected.

In sum, these data indicate that trichloroethylene produced some general toxicity (reduced body weight gain, increased relative liver and kidney weights) at all doses, while reducing reproductive indices only in the F_1 rats at the middle and high dose levels. Thus, trichloroethylene was not found to be a selective reproductive toxicant in rats.

Summary: NTP Reproductive Assessment by Continuous Breeding Study.

NTIS#: **PB86190782/AS**
Chemical: **Trichloroethylene**
CAS#: **79-01-6**
Mode of exposure: **Feed**
Species/strain: **Rat (F344)**

F_0 generation Dose concentration →	0.15%	0.30%	0.60%
General toxicity	Male, female	Male, female	Male, female
Body weight	—, ↓	—, ↓	↓, ↓
Kidney weight[a]	•	•	↑, ↑
Liver weight[a]	•	•	↑, ↑
Mortality	—, —	—, —	—, —
Feed consumption	—, —	—, —	—, —
Water consumption	•	•	•
Clinical signs	—, —	—, —	—, —
Reproductive toxicity			
x̄ litters/pair	—	—	—
# live pups/litter; pup wt./litter	—, —	↓, —	↓, —
Cumulative days to litter	—	—	—
Absolute testis, epididymis weight[a]	•	•	—, —
Sex accessory gland weight[a] (prostate, seminal vesicle)	•	•	—, —
Epidid. sperm parameters (#, motility, morphology)	•	•	—, —, —
Estrous cycle length	•	•	—

Determination of affected sex (crossover)	Male	Female	Both
Dose level	—	—	—

F_1 generation Dose concentration →	0.15%	0.30%	0.60%
General toxicity	Male, female	Male, female	Male, female
Pup growth to weaning	↓, ↓	↓, ↓	↓, ↓
Mortality	—, —	—, —	—, —
Adult body weight	↓, ↓	↓, ↓	↓, ↓
Kidney weight[a]	—, —	—, —	—, —
Liver weight[a]	↑, —	↑, ↑	↑, ↑
Feed consumption	—, —	—, —	—, —
Water consumption	•	•	•
Clinical signs	—, —	—, —	—, —
Reproductive toxicity			
Fertility index	—	—	—
# live pups/litter; pup wt./litter	—, —	—, —	—, —
Absolute testis, epididymis weight[a]	↓, —	↓, —	↓, —
Sex accessory gland weight[a] (prostate, seminal vesicle)	—, —	—, ↑	—, —
Epidid. sperm parameters (#, motility, morphology)	—, —, ↑	—, —, —	—, —, —
Estrous cycle length	•	•	•

Summary information	
Affected sex?	Unclear
Study confounders:	None
NOAEL reproductive toxicity:	0.15%
NOAEL general toxicity:	<0.15%
F_1 more sensitive than F_0?	No
Postnatal toxicity:	Yes

Legend: —, no change; •, no observation; ↑ or ↓, statistically significant change ($p<0.05$); —, —, no change in males or females. [a]Adjusted for body weight.